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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,203	03/13/2002	Tracey Brown	63370(49917)	8511
21874	7590	11/30/2006	EXAMINER	
EDWARDS & ANGELL, LLP			FUBARA, BLESSING M	
P.O. BOX 55874			ART UNIT	
BOSTON, MA 02205			PAPER NUMBER	

1618  
DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/889,203

Applicant(s)

BROWN, TRACEY

Examiner

Blessing M. Fubara

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

Examiner acknowledges receipt request for extension of time, declaration under 37 CFR 1.132, request for continued examination under 37 CFR 1.114 and remarks filed, all filed 9/11/06. Claims 1-9 are pending. Examiner thanks applicant for the declarations by Dr. Tracey.

#### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/11/2006 has been entered.

### **NEW MATTER**

#### ***Claim Rejections - 35 USC § 112***

2. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The recitation of hyaluronic acid having molecular weight of greater than or equal to 750,000 Daltons is new matter. Although applicants in the amendment that inserted the molecular indicated that there is support for the amendment in the specification as originally

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filed, the specific page and lines in the specification providing the support was not stated and Examiner does not find support for the amendment. There is also no support for HA having infinite molecular. Specific molecular weight, not ranges are disclosed.

Applicant's specification at page 39, line 31 has 700,000 kDa; page 40, line 16 has 700 kDa; page 29, line 28 has 890,000 kDa and page 17, line 37 has 890,000 kDa; the lower molecular weight range is thus not 750 kDa. Thus a molecular weight of equal to 750 kDa is new matter and has no support in the specification as originally filed.

### *Response to Arguments*

3. Applicant's arguments filed 9/11/06 have been fully considered but they are not persuasive..

Applicant refers to the following pages and lines for support for 750 kDa:

- a) page 17 line 37 gives  $8.9 \times 10^5$  kDa, which is = 890,000 kDa
- b) page 29, line 28 gives  $8.9 \times 10^5$  kDa, which is = 890,000 kDa
- c) page 39, line 31 gives  $7.5 \times 10^5$  kDa, which is = 750,000 kDa
- d) page 40, line 16 gives  $7 \times 10^5$  Da, which is = 700,000 Da, and this is 700 kDa

**Example 13 at page 79, line 35 does disclose 750 kDa; page 80 line 4 also gives 750 kDa.**

The above shows that there is one point where the HA has a weight of 750 kDa. However, there is no support for greater than since the greater than is open ended. As can be seen, there are definite points and the molecular weight is limited and in this case

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limited to an upper limit of 890,000 kDa. No range is disclosed. Greater than 750 kDa is not disclosed.

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Falk et al. (US 5,985,850).

Falk discloses injectable formulations comprising anti-cancer agent or chemotherapeutic agent and hyaluronic acid (column 10, lines 8-59). The preferred molecular weight for the hyaluronan is less than 750,000 Daltons (claims 142, 83, 84 and 92). Applicant's declaration is not commensurate with 750 kDa. Thus, the demonstration provided in applicant's declaration has no data at the lower end of 750 kDa and the 30 kDa data is much lower than 750 kDa. Therefore, there is no conclusive factual evidence that molecular weight equal to 750,000 Dalton provides unusual and unexpected results. Therefore, the evidence provided does not support hyaluronic acid having molecular weight of equal to 750,000 Daltons as being inventive over the disclosure in the prior art of a molecular weight of less than 750,000. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a composition comprising hyaluronic acid and anti-cancer agent to a subject in need thereof. One

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having ordinary skill in the art would have been motivated to use hyaluronic acid having the appropriate molecular weight that would provide the desired therapeutic effect and viscosity of the composition.

***Response to Arguments***

6. Applicant's arguments filed 9/11/06 have been fully considered but they are not persuasive.

Applicant argues that the HA of the invention is greater than or equal to 750 kDa

**Response:**

The molecular weight of the HA in the instant case a point where the HA is equal to 750 kDa and points where it is greater than 750 kDa. Thus the prior art 750 kDa touches the point where the molecular weight is at 750 kDa.

The declaration is not commensurate with the claims. The claimed hyaluronic acid has a molecular weight of equal to or greater than 750 kD. However, no data is provided at a molecular weight of 750 kDa or 700 kDa or outside of the upper limit if applicant considers upper limit. The 30 kDa is much lower than the claimed 750 kDa.

Declaration by Dr. Tracey Brown: The claim uses HA having molecular weight of greater than or equal to 750 kDa. The prior art molecular weight touches molecular weight equal to 750 kDa. The declaration is not also commensurate with the scope of the claim where  $\geq 750$  kDa is asserted. Since applicant has not provided an upper limit of what the molecular weight may be, it is no clear how the showing will be done at least at less than 750 kDa and

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greater than the upper limit. The disclosure has points at 890,000 kDa, 750,000 kDa, 700 kDa and 750 kDa.

These disclosed points may be considered in the factual evidence. Applicant may claim the upper limit to be as shown by the Dr. Tracey; these points are 880 and 1429. Dr. Tracey's data does not still have a point that is juts slightly lower that 750 kDa.

7. Claims 1-9 are rejected under in the alternative, under 35 U.S.C. 103(a) as obvious over Turley et al. (US 6,475,795 B1) in view of Sola et al. (US 6,214,860).

Turley discloses pharmaceutical composition that comprises anti-sense nucleic acid bound to hyaluronic acid for treating diseases or conditions treatable using gene therapy (column 6, line 60 to column 7 line 10; column 2, line 62 to column 3 line 7 and claims 1-8). Turley specifically discloses that hyaluronan having a molecular weight of between 150,000 Daltons and 750,000 Daltons is preferred (column 7, lines 11-15 and 33; column 9, lines 37-40; claims 2 and 3). In column 7, line 64, hyaluronan having molecular weight of between 500,000 and 800,000 is used and larger molecular weight hyaluronan can be used in Turley except for hyaluronan having molecular weight exceeding 1,000,000 because at greater that 1,000,000, the hyaluronan self aggregates (column 10, lines 7-14). On the basis that Turley discloses larger molecular weight hyaluronan up to 1,000,000 but not exceeding, 1,000,000, there is then a disclosure for use of hyaluronan having molecular weight of greater than 750,000 in the formulation of Turley. There is a disclosure for composition comprising hyaluronic acid having molecular weight of 500,000 to 800,000 Daltons and a composition that may have hyaluronan having preferred molecular weight of between 15,000 and 750,000 Daltons. Since molecular

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weight of 800,000 Daltons is greater than 750,000 Daltons, Turley renders obvious a molecular weight of greater than 750,000 Daltons is not inventive over the prior art. The declaration submitted by applicant is not commensurate with the claims.

Turley discloses anti-sense nucleic acid as the cytotoxic agent. Turley does not disclose non-polynucleic acid based cytotoxic agent. But one cytotoxic agent can be used in place of another with the expectation of producing antineoplastic effect. Sola recognizes paclitaxel, cisplatin and camptothecin as cytotoxic agents. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to inject a composition comprising hyaluronic acid and anti-sense agent to a subject in need thereof. One having ordinary skill in the art would have been motivated to use other cytotoxic agents such as paclitaxel, cisplatin and camptothecin as cytotoxic agents in place of the anti-sense nucleic acid with the expectation that these substitutes will provide antineoplastic effect.

### ***Response to Arguments***

8. Applicant's arguments filed 9/11/06 have been fully considered but they are not persuasive.

Applicant argues that Turley uses HA as a targeting agent for gene therapy and fails to disclose that the use of high molecular weight HA at > 750 kDa will have any effect at all on reducing or overcoming acquired or inherent cellular resistance. Applicant argues that Sola does not overcome the deficiencies of Turley. Applicant further argues that the office action improperly used hindsight reasoning.

### **Response:**

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HA is well known in the art and “[t]he discovery of a previously unappreciated property of prior art composition, or of a scientific explanation for the prior art’s functioning, does not render the old composition patentably new to the discoverer.” *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property, which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). Thus, because what the HA does is an inherent function of this well, the prior art does not have to disclose all the function of a known compound.

9. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

The motivation to combine Sola with Turley is that the use of cytotoxic agents such as paclitaxel, cisplatin and camptothecin cytotoxic agents in place of the anti-sense nucleic acid with the expectation of obtaining antineoplastic effect.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 7571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Blessing Fubara  
Patent Examiner  
Tech. Center 1600

A handwritten signature in black ink, appearing to read "Blessing Fubara", is written over the printed name and title of the examiner.